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=> file medline uspatfull wpids

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FILE 'WPIDS' ENTERED AT 16:33:18 ON 28 JUN 2001
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=> s hepatitis(w)B

L1       47079 HEPATITIS(W) B

=> s interferon?

L2       81306 INTERFERON?

=> s l1 and l2

L3        3852 L1 AND L2

=> s lamivudine

L4        1606 LAMIVUDINE

=> s l3(P)l4

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L9 (P)L13'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L10(P)L14'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L11(P)L15'
L5         135 L3(P) L4

=> s l3 and l4

L6         135 L3 AND L4

=> s adefovir

L7         154 ADEFOVIR

=> s l7 and l3

L8          15 L7 AND L3

=> s entecavir

L9           4 ENTECAVIR

=> s l9 and l3
```

L10 2 L9 AN B

=> d l10 1-2 bib ab

L10 ANSWER 1 OF 2 MEDLINE
AN 2001136209 MEDLINE
DN 20535646 PubMed ID: 11085196
TI Clinical potential of emerging new agents in **hepatitis B**
.
AU Farrell G C
CS Department of Medicine, University of Sydney at Westmead Hospital, New South Wales, Australia.. geoff_farrell@wmi.usyd.edu.au
SO DRUGS, (2000 Oct) 60 (4) 701-10. Ref: 60
Journal code: EC2; 7600076. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010223
Entered Medline: 20010301
AB Treatment of chronic **hepatitis B** is directed at interrupting the natural history and clinical outcomes of the disease. It needs to take into account the virology and replication cycle of the **hepatitis B** virus (HBV), and the host immune response to HBV. Long term follow-up of patients treated with **interferon** supports the paradigm that a sustained, major suppression of HBV replication, particularly that associated with **hepatitis B** e antigen (HBeAg) seroconversion, interrupts the natural history of **hepatitis B**. The availability of potent but well tolerated and orally available HBV antivirals, of which lamivudine is the prototype, has allowed clearer treatment objectives to be formulated. These are: temporary or permanent reduction of hepatitis (necroinflammatory) activity, arrest of fibrotic progression, prevention of cirrhosis and liver failure, and prevention of recurrent HBV infection after liver transplantation. Lamivudine has good medium term efficacy in achieving each of these objectives. The only significant problem for the longer term is emergence of antiviral resistance conferred by mutations in the YMDD (tyrosine-methionine-aspartic acid-aspartic acid) motif of the HBV reverse transcriptase. As a result, contentious issues remain about defining when antiviral therapy is indicated, whether to treat for a defined interval or indefinitely, and when to stop treatment if HBeAg seroconversion is not achieved. Some personal views are expressed in this review. Among newer HBV antivirals in clinical studies, adefovir dipivoxil, **entecavir** and emtricitabine appear to be at least as potent as lamivudine in suppressing HBV replication. Famciclovir appears less potent. In vitro studies show that YMDD mutations confer cross-resistance between lamivudine, emtricitabine and beta-L-Fd4C (L-2',3'-didehydro-dideoxy-5-fluorocytidine). However, adefovir dipivoxil, lobucavir, **entecavir**, DAPD (beta-D-2,6-diaminopurine dioxolane) and possibly clevudine (L-FMAU) suppress replication of YMDD mutant HBV, as well as wildtype. Preliminary studies indicate clinical efficacy of adefovir dipivoxil once resistance to lamivudine has developed. Immunomodulatory approaches to treatment of chronic **hepatitis B** are conceptually attractive, but newer agents used to date (thymalfasin, interleukin-12, therapeutic vaccines) have not demonstrated sufficient efficacy for widespread use. The next challenge for HBV

treatment is to use antivirals in combination and/or in cyclical therapy to reduce the emergence of drug resistance and increase efficacy, particularly to achieve sustainable post-treatment suppression of **hepatitis B**.

L10 ANSWER 2 OF 2 MEDLINE
AN 2000154339 MEDLINE
DN 20154339 PubMed ID: 10689749
TI [New developments in therapy of chronic **hepatitis B**. When are nucleoside analogs indicated?]. Neue Entwicklungen in der Therapie der chronischen **Hepatitis B**. Wann sind Nukleosidanaloga indiziert?.
AU Petry W; Erhardt A; Heintges T; Haussinger D
CS Klinik fur Gastroenterologie, Hepatologie und Infektiologie, Heinrich-Heine-Universitat Dusseldorf.
SO ZEITSCHRIFT FUR GASTROENTEROLOGIE, (2000 Jan) 38 (1) 77-87. Ref: 61
Journal code: XU1; 0033370. ISSN: 0044-2771.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 200003
ED Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000322
AB Nucleoside analogues are promising agents for the treatment of chronic **hepatitis B** infection (HBV-DNA-positive by hybridization assay). The drug being studied most intensively is Lamivudine (Zeffix) which has recently been approved in Germany. When given orally once daily (100 mg) Lamivudine is well-tolerated and suppresses HBV-DNA to undetectable levels in the majority of patients. Since relapse is frequent when medication is stopped long-term treatment (at least until seroconversion of HBeAg) is warranted. Indications for lamivudine monotherapy are patients with chronic **hepatitis B** in which **interferon** (IFN) is contraindicated or patients who did not respond to a previous course of **interferon**. Further indications are the HBV-DNA-positive cirrhosis prior to liver transplantation (OLT) and the HBV-reinfection after OLT. The main problem of long-term monotherapy with lamivudine is viral resistance. The clinical impact of the resistant mutants is often not clear. Withdrawal or even continuation of the medication may be acceptable approaches. Other nucleoside analogues like **Entecavir** or Adefovir are currently being tested in clinical studies. Famciclovir was investigated preferably in patients with decompensated liver disease or HBV-reinfection after OLT.
Because of conflicting results the drug should only be used under study conditions. In IFN-naive patients with chronic **hepatitis B** (and compensated liver disease) alpha-**interferon** is still the first-line therapy. With a standard course of **interferon** 30-40% of the patients become seronegative for HBeAg as compared with 16-17% when treated with lamivudine for twelve months. Combination of lamivudine and **interferon** is not more effective than IFN alone. In the future combined antiviral treatment is likely to replace monotherapy.

=> d l8 1-15 bib ab

L8 ANSWER 1 OF 15 MEDLINE
AN 2001188982 MEDLINE

DN 21175123 PubMed ID: 11279893
TI [Current treatment of **hepatitis B**].
Tratamiento actual de la **hepatitis B**.
AU Suarez Garcia E; Romero Gomez M; Grande Santamaria L
CS Seccion de Aparato Digestivo, Hospital Universitario de Valme, Sevilla.
SO GASTROENTEROLOGIA Y HEPATOLOGIA, (2001 Feb) 24 Suppl 1 35-50.
Journal code: CE5; 8406671. ISSN: 0210-5705.
CY Spain
DT Journal; Article; (JOURNAL ARTICLE)
LA Spanish
FS Priority Journals
EM 200104
ED Entered STN: 20010502
Last Updated on STN: 20010502
Entered PubMed: 20010330
Entered Medline: 20010426

L8 ANSWER 2 OF 15 MEDLINE
AN 2001136209 MEDLINE
DN 20535646 PubMed ID: 11085196
TI Clinical potential of emerging new agents in **hepatitis B**
.
AU Farrell G C
CS Department of Medicine, University of Sydney at Westmead Hospital, New South Wales, Australia.. geoff_farrell@wmi.usyd.edu.au
SO DRUGS, (2000 Oct) 60 (4) 701-10. Ref: 60
Journal code: EC2; 7600076. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010223
Entered Medline: 20010301
AB Treatment of chronic **hepatitis B** is directed at interrupting the natural history and clinical outcomes of the disease. It needs to take into account the virology and replication cycle of the **hepatitis B** virus (HBV), and the host immune response to HBV. Long term follow-up of patients treated with **interferon** supports the paradigm that a sustained, major suppression of HBV replication, particularly that associated with **hepatitis B** e antigen (HBeAg) seroconversion, interrupts the natural history of **hepatitis B**. The availability of potent but well tolerated and orally available HBV antivirals, of which lamivudine is the prototype, has allowed clearer treatment objectives to be formulated. These are: temporary or permanent reduction of hepatitis (necroinflammatory) activity, arrest of fibrotic progression, prevention of cirrhosis and liver failure, and prevention of recurrent HBV infection after liver transplantation. Lamivudine has good medium term efficacy in achieving each of these objectives. The only significant problem for the longer term is emergence of antiviral resistance conferred by mutations in
the YMDD (tyrosine-methionine-aspartic acid-aspartic acid) motif of the HBV reverse transcriptase. As a result, contentious issues remain about defining when antiviral therapy is indicated, whether to treat for a defined interval or indefinitely, and when to stop treatment if HBeAg seroconversion is not achieved. Some personal views are expressed in this review. Among newer HBV antivirals in clinical studies, **adefovir** dipivoxil, entecavir and emtricitabine appear to be at least as potent as lamivudine in suppressing HBV replication. Famciclovir appears less potent. In vitro studies show that YMDD mutations confer cross-resistance

between lamivudine, emtricitabine and beta-L-Fd4C (L-2',3'-didehydro-dideoxy-5-fluorocytidine). However, **adefovir** dipivoxil, lobucavir, entecavir, DAPD (beta-D-2,6-diaminopurine dioxolane) and possibly clevudine (L-FMAU) suppress replication of YMDD mutant HBV, as well as wildtype. Preliminary studies indicate clinical efficacy of **adefovir** dipivoxil once resistance to lamivudine has developed. Immunomodulatory approaches to treatment of chronic **hepatitis B** are conceptually attractive, but newer agents used to date (thymalfasin, interleukin-12, therapeutic vaccines) have not demonstrated sufficient efficacy for widespread use. The next challenge for HBV treatment is to use antivirals in combination and/or in cyclical therapy to reduce the emergence of drug resistance and increase efficacy, particularly to achieve sustainable post-treatment suppression of **hepatitis B**.

L8 ANSWER 3 OF 15 MEDLINE
AN 2000513349 MEDLINE
DN 20522359 PubMed ID: 11070570
TI Chronic viral hepatitis.
AU Alexander G; Walsh K
CS Department of Medicine, Addenbrooke's Hospital, Cambridge, UK.
SO INTERNATIONAL JOURNAL OF CLINICAL PRACTICE, (2000 Sep) 54 (7) 450-6.
Ref:
92
Journal code: CVT. ISSN: 1368-5031.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001120
AB Both **hepatitis B** and hepatitis C are spread parenterally. Chronic hepatitis C is fast becoming the leading indication for liver transplantation. Most infected patients go on to develop chronic hepatitis, with approximately 20% developing liver cirrhosis or hepatocellular carcinoma after 20 years. Standard treatment now is with a combination of alpha-**interferon** and ribavirin, which is successful in up to 40% of patients. A vaccine is still a remote possibility and prevention remains all-important. Despite having a successful vaccine, chronic **hepatitis B** remains an important cause of liver cirrhosis and hepatocellular carcinoma. Treatments for active hepatitis include alpha-**interferon** and the newer nucleoside analogues such as lamivudine and **adefovir**. In patients undergoing liver transplantation, recurrence of **hepatitis B** in the graft can be reduced with a combination of **hepatitis B** immunoglobulin and these nucleoside analogues.

L8 ANSWER 4 OF 15 MEDLINE
AN 2000474693 MEDLINE
DN 20392635 PubMed ID: 10936954
TI [Diagnosis and treatment of **hepatitis B**].
Diagnostico e tratamento da hepatite B.
AU Ferreira M S
CS Disciplina de Doencas Infecciosas e Parasitarias, Universidade Federal de Uberlandia, MG, Brasil.
SO REVISTA DA SOCIEDADE BRASILEIRA DE MEDICINA TROPICAL, (2000 Jul-Aug) 33 (4) 389-400. Ref: 50
Journal code: RET; 7507456. ISSN: 0037-8682.
CY Brazil

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Portuguese
FS Priority Journals
EM 200010
ED Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001003
AB **Hepatitis B** constitutes a serious public health problem. It has been estimated that 350 million people--approximately 5% of the world population--have been infected by this virus. Of the people infected, in 90% to 95% of them there will be a spontaneous resolution of the disease. In 5% to 10% of the cases, though, the infection will persist and a chronic hepatitis will develop that may evolve leading, in the end, to liver cirrhosis, liver failure and/or carcinoma of the liver. The diagnosis of the different stages of the disease (i.e., acute, chronic infection) is performed using modern serologic techniques. Physicians, more recently, are having access to a series of laboratory tests which permit them to evaluate the viral load, replication of the virus and to testing of the efficacy of new anti-viral drugs. For the treatment of chronic **hepatitis B** new agents have been tested and some are being used with different degrees of success, such as, alfa-**interferon**, lamivudine, famciclovir, and **adefovir** dipivoxil, among others. Active immunization, using modern recombinant vaccines, are lately, the most important instrument of control of the infection caused by the **hepatitis B** virus.

L8 ANSWER 5 OF 15 MEDLINE
AN 2000324752 MEDLINE
DN 20324752 PubMed ID: 10868900
TI Antiviral chemotherapy for the treatment of **hepatitis B** virus infections.
AU Torresi J; Locarnini S
CS Victorian Infectious Diseases Reference Laboratory, North Melbourne, Australia.
SO GASTROENTEROLOGY, (2000 Feb) 118 (2 Suppl 1) S83-103. Ref: 194
Journal code: FH3; 0374630. ISSN: 0016-5085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200007
ED Entered STN: 20000714
Last Updated on STN: 20000714
Entered Medline: 20000706
AB Approximately 5% of the world's human population have an increased risk for developing liver cancer and cirrhosis as a direct consequence of chronic infection with the **hepatitis B** virus (HBV). Antiviral chemotherapy remains the only option for controlling infection in these individuals, for whom the current licensed **hepatitis B** vaccines provide no benefit. **Interferon** (IFN)-alpha has proven benefit in a well-defined group of those with **hepatitis B** but has made little impact on the global burden of chronic liver disease. The development of more effective chemotherapy for treatment of chronic **hepatitis B** infection has proven to be extremely challenging, the result of both virus- and host-dependent factors, which will be reviewed in this article. Past attempts to treat chronic **hepatitis B** infection using nucleoside analogues were disappointing, but more recently, several nucleoside (or nucleotide) analogues have been identified that are potent and selective inhibitors of HBV replication. These agents fall into two broad

categories: (1) nucleoside/nucleotides that have modified sugar residues in either cyclic or acyclic configurations and (2) stereoisomers of nucleosides in the "unnatural" L-configuration. Of the analogues that have been used clinically, representatives of the first category are purine derivatives, e.g., **adefovir** dipivoxil and famciclovir, whereas representatives of the second category are pyrimidine derivatives, such as lamivudine.

L8 ANSWER 6 OF 15 MEDLINE
AN 2000192814 MEDLINE
DN 20192814 PubMed ID: 10730571
TI Therapy of chronic viral hepatitis: a critical view.
AU Rizzetto M
CS Department of Gastroenterology, University of Turin, Italy.
SO ITALIAN JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (1999 Nov) 31 (8) 781-93. Ref: 127
Journal code: CVR; 9711056. ISSN: 1125-8055.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000405
AB Many oral nucleoside analogues that are potent inhibitors of **hepatitis B** virus have recently been developed for the treatment of **hepatitis B**. The problems with these drugs are bioavailability, toxicity and the time-dependent emergence of resistant **hepatitis B** virus mutants. Lamivudine appears to be the most useful in terms of clinical benefit, safety and tolerance. It is active on wild type **hepatitis B** virus as well as on HBeAg-minus variants of the virus. However, although **hepatitis B** virus is consistently repressed while on therapy, only a minority of patients are cured or remain in remission after Lamivudine withdrawal. Maintenance therapy would appear to be in order, but the long-term use of Lamivudine is precluded by the emergence of polymerase gene-mutants which may rekindle disease. Combination with other antivirals (**Adefovir**?) active also against Lamivudine escape mutants opens promising new prospects. There is, as yet, no valid therapy for chronic hepatitis D virus hepatitis. Attempts to improve the results of alpha-**interferon** therapy in chronic hepatitis C with new **interferons**, or the manipulation of **interferon** monotherapy so as to obtain the maximum results compatible with tolerance, have not produced significantly better results than the classic protocols of alpha-**interferon** monotherapy. A more concrete improvement has been achieved by the combination of **interferon** with Ribavirin, with the overall rate of response increasing three times compared to **interferon** monotherapy. Anaemia, however, is a common additional side-effect induced by Ribavirin. Combination therapy has become the treatment of choice for **interferon** naive patients as well as for **interferon** relapses; it is not efficacious in patients who have not responded to **interferon**.

L8 ANSWER 7 OF 15 MEDLINE
AN 2000154339 MEDLINE
DN 20154339 PubMed ID: 10689749
TI [New developments in therapy of chronic **hepatitis B**. When are nucleoside analogs indicated?].
Neue Entwicklungen in der Therapie der chronischen **Hepatitis**

B. Wann sind Nukleosidanaloga indiziert?.
AU Petry W; Erhardt [redacted] Heintges T; Haussinger D
CS Klinik fur Gastroenterologie, Hepatologie und Infektiologie, Heinrich-Heine-Universitat Dusseldorf.
SO ZEITSCHRIFT FUR GASTROENTEROLOGIE, (2000 Jan) 38 (1) 77-87. Ref: 61
Journal code: XU1; 0033370. ISSN: 0044-2771.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 200003
ED Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000322
AB Nucleoside analogues are promising agents for the treatment of chronic **hepatitis B** infection (HBV-DNA-positive by hybridization assay). The drug being studied most intensively is Lamivudine (Zeffix) which has recently been approved in Germany. When given orally once daily (100 mg) Lamivudine is well-tolerated and suppresses HBV-DNA to undetectable levels in the majority of patients. Since relapse is frequent when medication is stopped long-term treatment (at least until seroconversion of HBeAg) is warranted. Indications for lamivudine monotherapy are patients with chronic **hepatitis B** in which **interferon** (IFN) is contraindicated or patients who did not respond to a previous course of **interferon**. Further indications are the HBV-DNA-positive cirrhosis prior to liver transplantation (OLT) and the HBV-reinfection after OLT. The main problem of long-term monotherapy with lamivudine is viral resistance. The clinical impact of the resistant mutants is often not clear. Withdrawal or even continuation of the medication may be acceptable approaches. Other nucleoside analogues like Entecavir or **Adefovir** are currently being tested in clinical studies. Famciclovir was investigated preferably in patients with decompensated liver disease or HBV-reinfection after OLT.
Because of conflicting results the drug should only be used under study conditions. In IFN-naive patients with chronic **hepatitis B** (and compensated liver disease) alpha-**interferon** is still the first-line therapy. With a standard course of **interferon** 30-40% of the patients become seronegative for HBeAg as compared with 16-17% when treated with lamivudine for twelve months. Combination of lamivudine and **interferon** is not more effective than IFN alone. In the future combined antiviral treatment is likely to replace monotherapy.

L8 ANSWER 8 OF 15 MEDLINE
AN 1999310004 MEDLINE
DN 99310004 PubMed ID: 10382631
TI Update on clinical trials in the treatment of **hepatitis B**.
AU Pessoa M G; Wright T L
CS Department of Veterans Affairs Medical Center, University of California, San Francisco 94121, USA.
SO JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (1999 May) 14 Suppl S6-11. Ref: 30
Journal code: A6J; 8607909. ISSN: 0815-9319.
CY Australia
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals

EM 199908
ED Entered STN: 19[redacted]827
Last Updated on STN: 19990827
Entered Medline: 19990817
AB Chronic **hepatitis B** infection is a worldwide public health problem, which is particularly important in countries of Asia. **Interferon** has long been available for the treatment of patients with active replication (**hepatitis B** virus (HBV) e antigen and HBV-DNA positive) with evidence of chronic liver disease (elevated serum alanine aminotransferase and chronic hepatitis on liver biopsy). Doses of **interferon** of 10 MU, t.i.w. or 5 MU, q day for 16 weeks result in e antigen and HBV-DNA loss in approximately one-third of individuals who meet these treatment criteria. The major limitations of **interferon** are: (i) side effects of influenza-like symptoms; (ii) need for parenteral administration; and (iii) concerns about safety in patients with hepatic decompensation. Nucleoside and nucleotide analogues have potent antiviral activity. The largest experience is with lamivudine (3-thiacytadine), a reverse transcriptase inhibitor that was recently approved by the USA Federal Drug Administration. At doses of 100 mg/day for 52 weeks, suppression of HBV replication is almost universal, with e antigen loss and improvement in histology being achieved in one-third and two-thirds of patients, respectively. The major advantages of lamivudine are: (i) good tolerability; (ii) oral route of administration; and (iii) safety in patients with hepatic decompensation. The major disadvantage is drug resistance, which is observed with increasing frequency following prolonged administration. New agents, such as **adefovir** dipivoxil, offer promise either alone or in combination with lamivudine in the treatment of individuals who are 'treatment naive' as well as in the treatment individuals who have developed lamivudine resistance.

L8 ANSWER 9 OF 15 MEDLINE
AN 1998163425 MEDLINE
DN 98163425 PubMed ID: 9504896
TI Review: Present and future directions in the treatment of chronic **hepatitis B** infection.
AU Nicoll A; Locarnini S
CS Victorian Infectious Diseases Reference Laboratory, Fairfield Hospital, Victoria, Australia.
SO JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (1997 Dec) 12 (12) 843-54.
Ref: 134
Journal code: A6J; 8607909. ISSN: 0815-9319.
CY Australia
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980430
AB The last decade has witnessed substantial progress in the development of chemotherapeutic agents for chronic **hepatitis B**. However, the only currently licensed treatment in Australia, **interferon**-alpha, has low initial response rates and the adverse effects are often unacceptable. Of the newer agents in the class of nucleoside analogues, famciclovir and lamivudine are in phase III clinical trials with encouraging preliminary results, while other agents, such as bis-POM PMEA (**Adefovir**), are at phase I/II development. Future approaches to therapy will be governed by an understanding of the effects of nucleoside analogues on the natural history of the disease as well as on the **hepatitis B** virus hepatocyte interaction.

Combination antiviral therapy should theoretically offer improved response
rates, decrease the development of viral resistance, and provide the greatest reduction in viral load, but it has not yet been widely examined in the clinical setting. In this article, we review the currently available strategies, discuss potential problem areas, and speculate on promising approaches with combination chemotherapy and the features of agents soon to be trialed.

L8 ANSWER 10 OF 15 USPATFULL
AN 2001:90260 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PI US 2001002404 A1 20010531
AI US 2000-730450 A1 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DT Utility
LREP Edward R. Gates, Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2511
AB The invention provides conjugates of fatty acids and pharmaceutical agents useful in treating noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

L8 ANSWER 11 OF 15 USPATFULL
AN 2001:33274 USPATFULL
TI Synthesis, anti-human immunodeficiency virus, and anti-**hepatitis B** virus activities of 1,3-oxaselenolane nucleosides
IN Schinazi, Raymond F., Decatur, GA, United States
Chu, Chung K., Athens, GA, United States
Du, Jinfa, Irvine, CA, United States
PA Emory University, Atlanta, GA, United States (U.S. corporation)
The University of Georgia Research Foundation, Inc., Athens, GA, United States (U.S. corporation)
PI US 6197777 B1 20010306
AI US 2000-517955 20000303 (9)
RLI Division of Ser. No. US 1998-44558, filed on 19 Mar 1998, now patented, Pat. No. US 6071922
PRAI US 1997-41265 19970319 (60)
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Truong, Tamthom N.
LREP Knowles, Esq., Sherry M.King & Spalding
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1668
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method and composition for the treatment of HIV infection, HBV infection, or abnormal cellular proliferation in humans and other host animals is disclosed that includes the administration of an effective amount of a 1,3-oxaselenolane nucleoside or a pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier.

L8 ANSWER 12 OF 15 USPATFULL
AN 2001:29543 USPATFULL

TI 3'-azido-2',3'-dideoxyuridine administration to treat HIV and related test protocol
IN Schinazi, Raymond F., Decatur, GA, United States
Bryant, Martin L., Carlisle, MA, United States
Myers, Maureen W., Carlisle, MA, United States
PA Emory University, Atlant, GA, United States (U.S. corporation)
Norvirio Pharmaceuticals Limited, Grand Cayman, Cayman Islands (non-U.S. corporation)
PI US 6194391 B1 20010227
AI US 1999-339133 19990624 (9)
PRAI US 1998-90552 19980624 (60)
US 1999-132126 19990430 (60)
DT Utility
EXNAM Primary Examiner: Killos, Paul J.; Assistant Examiner: Crane, L. E.
LREP Knowles, Sherry M.King & Spalding
CLMN Number of Claims: 32
ECL Exemplary Claim: 1,10,11
DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 2273
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB It has been discovered that 3'-azido-2',3'-dideoxyuridine (CS-87) induces a transient mutation in HIV-1 at the 70.sup.th codon (K to R, i.e., lysine to arginine) of the reverse transcriptase region of the virus. Based on this discovery, a method and composition for treating HIV is provided that includes administering CS-87 or its pharmaceutically acceptable salt or prodrug to a human in need of therapy in combination or alternation with a drug that induces a mutation in HIV-1 at a location other than the 70.sup.th codon of the reverse transcriptase region. This invention can be practiced by referring to the published mutation patterns for known anti-HIV drugs, or by determining the mutation pattern for a new drug.

L8 ANSWER 13 OF 15 USPATFULL
AN 2000:70851 USPATFULL
TI Synthesis, anti-human immunodeficiency virus, and anti-**hepatitis B** virus activities of 1,3-oxaselenolane nucleosides
IN Schinazi, Raymond F., Decatur, GA, United States
Chu, Chung K., Athens, GA, United States
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PA Emory University, Atlanta, GA, United States (U.S. corporation)
The University of Georgia Research Foundation, Inc., Athens, GA, United States (U.S. corporation)
PI US 6071922 20000606
AI US 1998-44558 19980319 (9)
PRAI US 1997-41265 19970319 (60)
DT Utility
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Truong, Tamthom N.
LREP Knowles, Sherry M., Haley, JacquelineKing & Spalding
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1780
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method and composition for the treatment of HIV infection, HBV infection, or abnormal cellular proliferation in humans and other host animals is disclosed that includes the administration of an effective amount of a 1,3-oxaselenolane nucleoside or a pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier.

L8 ANSWER 14 OF 15 USPATFULL
AN 1998:98932 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes

IN Shashoua, Vic[redacted] E., Brookline, MA, United Sta[redacted]
Swindell, Cha[redacted]s S., Merion, PA, United State[redacted]
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5795909 19980818
AI US 1996-651312 19960522 (8)
DT Utility
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and taxanes useful in treating cell proliferative disorders. Conjugates of paclitaxel and docetaxel are preferred.

L8 ANSWER 15 OF 15 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-490988 [43] WPIDS
DNC C2000-147537
TI Treatment and prevention of **hepatitis B** virus infection, using an antiviral agent and a vaccine in simultaneous or sequential use.
DC A96 B04 B05 D16
IN ATKINSON, G F; BOON, R J; VANDEPAPELIERE, P G; WETTENDORFF, M A C
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 90
PI WO 2000041463 A2 20000720 (200043)* EN 18p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 2000021009 A 20000801 (200054)
ADT WO 2000041463 A2 WO 1999-EP10295 19991221; AU 2000021009 A AU 2000-21009 19991221
FDT AU 2000021009 A Based on WO 200041463
PRAI GB 1999-630 19990112
AB WO 200041463 A UPAB: 20000907
NOVELTY - Pharmaceutical pack comprising an antiviral agent active against **hepatitis B** virus (HBV), and a vaccine for the prophylaxis and/or treatment of **hepatitis B** infection, for simultaneous or sequential use, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) treating a patient suffering from or susceptible to HBV infection, comprising administering either simultaneously or sequentially in any order, an antiviral agent active against HBV, and a vaccine for the prophylaxis and/or treatment of **hepatitis B** infection;
(2) use of an antiviral compound in the manufacture of a medicament for the treatment of patients already primed with a **hepatitis B** vaccine or an antiviral compound, and suffering from a HBV infection; and
(3) use of a **hepatitis B** vaccine in the manufacture of a medicament for the treatment of patients already primed with an antiviral compound and suffering from a HBV infection.
ACTIVITY - Antiviral; hepatotropic; antinflammatory; immunostimulatory.
MECHANISM OF ACTION - Vaccine.
USE - The pharmaceuticles can be used to treat and prevent

hepatitis B infections.
Dwg.0/0